Keep on taking the medicine?

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How do you help someone who doesn't see the point of taking their medication? Parastou Donyai considers strategies for understanding and tackling medication non-adherence

Imagine a patient who is 60 and recovering from breast cancer. She was treated in hospital with surgery, chemotherapy and radiotherapy six months ago. She was then sent home with letrozole tablets, a hormonal treatment, and told to take them once a day for the next five years. Since starting the letrozole tablets, she has been experiencing night sweats, hot flushes and headaches. She complains that the GP, although very nice, doesn't want to discuss her medication with her as this is related to her cancer which 'the hospital treated'. She tells you that she's unlikely to continue with her medication for much longer, seeing that taking letrozole will mean spoiling the last 'good five years' of her life. How would you respond?

Medication is the most common intervention in healthcare. Community pharmacies dispensed over a thousand million prescribed items in England in 2015; an average of 20 items for every inhabitant. Scotland and Northern Ireland had a similar average with Wales pharmacies dispensing 26 items for each inhabitant. This is perhaps to be expected as prescribers use medication to prevent, treat or manage a range of conditions. Consider that there is a large proportion of elderly people in the UK and they are likely to have medical conditions needing treatment. Also, across the population people have different chronic conditions, such as diabetes, which are managed with medication. In addition, a number of guidelines encourage doctors to prescribe medicines to prevent illnesses; for example, lipid-lowering medication to reduce the risk of stroke or heart attacks. In relation to the 60-year old patient described above, the National Institute for Health and Care Excellence (NICE) recommends prescribing aromatase inhibitors (a form of hormonal treatment) such as letrozole to delay the return of cancer and increase overall survival in women who receive treatment for early-stage breast cancer after the menopause.

Medicines for conditions affecting the mind and the nervous system (e.g. mental health conditions) cost the most, followed by conditions affecting the endocrine (e.g. diabetes), respiratory (e.g. asthma), and cardiovascular (e.g. high blood pressure) systems. Items dispensed in England in 2015 had a Net Ingredient Cost of £9,266.6 million. Despite the expenditure, people commonly fail to take their dispensed medication as instructed. This article asks what progress has been made in understanding and tackling medication-taking behaviour since the subject was last covered by *The Psychologist* over a decade ago in 2005.

Definition of adherence

We are going to use the term *medication adherence* when referring to medication-taking behaviour—instead of *medication compliance*, which carries a negative inference of passive obedience (Sabaté, 2003). Medication adherence is about how the patient takes their medication compared with the instructions on their prescription. There are three stages to adherence. The first is the initiation stage which is whether the patient takes the first dose as prescribed. Next is the implementation stage which is '*the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose is taken*'. The final stage is the discontinuation stage which is whether the patient takes the last dose as prescribed (Vrijens, et al., 2012). Another key term is persistence, which is the length of time between the initiation stage and the discontinuation stage. A patient can be non-adherent to their medication regimen if they fail to collect and take their medication on time,

if at all (described as *primary non-adherence*), if they don't follow the dosing regimen during the implementation stage (*secondary non-adherence*), and if they discontinue the course early (*non-persistence*). One other term for us to consider is *concordance*. It describes a medical consultation process whereby the prescriber and patient agree therapeutic decisions that incorporate both views, and the term also encompasses prescriber communication and patient support in medicine taking (Horne, et al., 2005).

The extent of the problem

The World Health Organisation estimated in 2003 that patients do not take between 30-50% of medicines prescribed for long-term conditions as intended, and this remains an often-used statistic to depict the extent of the medication non-adherence problem (Sabaté, 2003). Measuring the true prevalence of medication non-adherence in chronic conditions has been particularly difficult because no methodological gold standard exists to measure the range of non-adherent behaviours (Vermeire, Hearnshaw, Van Royen, & Denekens, 2002). Researchers have used subjective methods (e.g. by asking the patient to report their adherence), objective approaches (e.g. by using electronic monitoring devices to record doses accessed, or pharmacy databases to look at the frequency of dispensing), as well as direct methods (e.g. biochemically measuring the amount of drug in the patient's body, or placing a microchip inside the medication form) to quantify adherence behaviour, but none is a perfect instrument (Dodds, Rebair-Brown, & Parsons, 2000). In addition, researchers have used different ways to quantify adherence, calculating for example, the proportion of prescribed drug taken, days with correct number of doses, doses taken on time, or the number of drug holidays, and so on (Vrijens, et al., 2012). This heterogeneity in measurement means it is difficult to accurately compare adherence between different conditions.

However, we can draw on a useful US study which compared adherence and persistence across 6 chronic medication classes using one methodology. It found variable but uniformly suboptimal use with medication prescribed for diabetes (mean 12-month adherence rate 72%), overactive bladder (35%), cholesterol (61%), cardiovascular disease (66%), osteoporosis (60%), and glaucoma (37%) (Yeaw, Benner, Walt, Sian, & Smith, 2009). Other chronic conditions where patients are known to be non-adherent include Human Immunodeficiency Virus (HIV), arthritis, gastrointestinal disorders, cancer, pulmonary disease, mental health disorders and epilepsy (DiMatteo, Giordani, Lepper, & Croghan, 2002; Sabaté, 2003). When people don't adhere to their medication this can reduce the clinical benefit of the medication and in turn affect the patient's quality of life. Medication non-adherence affects health systems by increasing the burden of ill health, medicines waste, hospitalisation and emergency admission as well as death (Simpson, et al., 2006; DiMatteo, Giordani, Lepper, & Croghan, 2002).

The Psychology

Some consider medication non-adherence to be either unintentional (e.g. due to forgetfulness or carelessness) or intentional (e.g. not believing in the treatment) although this is an over-simplification since people's beliefs can also predict unintentional non-adherence (Gadkari & McHorney, 2012). One psychological model of medication adherence is the Necessity-Concerns Framework, which concentrates on intentional non-adherence. At its heart is the idea that patients' common-sense beliefs about prescribed medicines can be captured and categorised according to *necessity beliefs*, perceptions of personal need for treatment, and *concerns* about a range of potential adverse consequences—and that intentional adherence is

associated with greater necessity beliefs versus concerns (Horne, R; Weinman, J, 1999). The associated *Beliefs about Medicines Questionnaire* quantifies necessity beliefs and concerns (Horne, R; Weinman, J; Hankins, M, 1999) with its originators encouraging healthcare professionals to use it within clinical consultations to elicit and respond to patient beliefs (Horne, et al., 2013). Other tools for screening non-adherence across chronic diseases also exist (Svarstad, Chewning, Sleath, & Claesson, 1999; Willey, et al., 2000; George, Mackinnon, Kong, & Stewart, 2006; Hahn, et al., 2008; McHorney, 2009). However, it is important to note that practitioners as a whole have not adopted any of these tools widely in practice and non-adherence remains a complex problem that is yet unresolved.

A multitude of studies have examined the psychological causes of non-adherence across chronic health conditions and patient characteristics, emphasising different factors such as the severity of the disease and whether symptoms are present, patients' perception of their condition and sense of vulnerability, their concerns about medication side-effects and long-term consequences, their knowledge about a medicine's mechanism of action, and their health literacy in general, the complexity of the regimen, patient forgetfulness, their fear of dependence, and so on (Sabaté, 2003; Vermeire, Hearnshaw, Van Royen, & Denekens, 2002; Pound, et al., 2005; Kardas, Lewek, & Matyja, 2013). This reflects the current understanding that the reasons for non-adherence are multifaceted and not easy to categorise.

The World Health Organisation (WHO) report on adherence described five interacting dimensions of non-adherence to be healthcare system/team factors, patient-related factors, therapy-related factors, condition-related factors, and social and economic factors (Sabaté, 2003). The WHO report defined patient-related factors of adherence to be the resources, knowledge, attitudes, beliefs, perceptions and expectations of the patient (Sabaté, 2003). It identified the major patient-related barriers to adherence to be lack of information and skills as they relate to self-management, difficulty with motivation and self-efficacy, and lack of support for behavioural changes (Sabaté, 2003). The report advocated the development of self-management interventions aimed at improving motivation and adherence noting that '*patients need to be informed, motivated and skilled in the use of cognitive and behavioural self-regulation strategies if they are to cope effectively with the treatment-related demands imposed by their illness'* (Sabaté, 2003).

The Evidence

A 2014 Cochrane review examined 182 randomised controlled trials (RCTs) of interventions to improve adherence with prescribed medications, measuring both medication adherence and clinical outcomes (Nieuwlaat, et al., 2014). It found that researchers most frequently targeted conditions including HIV/AIDS, psychiatric disorders, chronic obstructive pulmonary disease, cardiovascular disease or cardiovascular risk, hypertension, and diabetes. The Cochrane reviewers identified seventeen studies as having a low risk of bias with only five reporting improvements in both adherence and clinical outcomes; three improved only adherence outcomes, one improved only clinical outcomes, and the remainder did not improve adherence or clinical outcomes. They found no study that led to large improvements and also found no obvious common study characteristics. The authors noted the most robust designs generally involved complex interventions with multiple components, where healthcare professionals (e.g. pharmacists) gave ongoing tailored support, often delivering intense education, counselling (including motivational interviewing or cognitive behavioural therapy by professionals) or daily treatment support (or both), and sometimes there was additional support from family or peers (Nieuwlaat, et al., 2014). However, the reviewers could not make a judgement about which intervention type was most effective because of the

diversity and complexity of the studies (e.g. the variety of settings, participants, intervention types, medications, adherence measures, and clinical outcome).

The European ABC project also reviewed RCTs but included only studies where researchers had assessed adherence by electronic medication-event monitoring—this consists of an automatic, electronically-compiled drug dosing history for each patient (Demonceau, et al., 2013). The ABC's systematic reviewers examined the determinants of adherence using a multiple regression model as well as a meta-analysis. Both the multiple regression model and the meta-analysis found statistically significant increases in adherence when the intervention included feedback to patients using electronic monitoring, *EM-feedback*, or involved a cognitive-educational component *Cogn-Educ*. To elaborate, *EM-feedback* involved a focused discussion based on giving feedback to the patient of his/her recent dosing history data, as a guided example of behavioural-counselling. *Cogn-Educ* interventions presented information individually or in a group setting, verbally, in written form, and/or audiovisually, in order to educate and motivate patients—the rationale is that patients who understand their condition and its treatment will be more informed, more empowered and more likely to adhere. The ABC's systematic reviewers also examined and reported on intervention components (Demonceau, et al., 2013). For example, studies using rewards although demonstrated median improvement, had a small sample size and thus did not demonstrate statistical significance. The other techniques that also did not demonstrate clinical significance included treatment simplification, behavioural-counselling interventions, social-psycho-affective interventions, technical reminder systems, and providing technical equipment for disease monitoring.

The research in this area is complex and conflicting. For example, an earlier systematic review of adherence in chronic conditions found the most effective interventions to be those that simplify dosing demands as well as those involving monitoring and feedback, and multisession informational trials (Kripalani, Yao, & Haynes, 2007). A meta-review of over 1,300 original articles also concluded that effective adherence interventions include technical solutions such as simplifications of dosage and packaging (van Dulmen, et al., 2007). Perhaps the common thread to all reviews of medication-adherence interventions is that there is no consistent quantifiable evidence of effectiveness associated with any particular intervention type. We might form the view that there is a need for further research to provide more robust evidence linking behaviour-change interventions with improved adherence, e.g. leading either to a large improvement in adherence or in clinical outcomes. But another view we might form is that the factors of non-adherence are so complex, that no single intervention or package of interventions could ever be effective across patients, conditions and settings. It would follow that instead of pursuing a truth-seeking, reductionist search for effective interventions we should focus on providing a concordant, client-centred approach to medicines adherence by listening to our patients and addressing their concerns.

The advice

In keeping with a client-centred approach, the current National Institute for Health and Care Excellence (NICE) guideline on medicines adherence makes recommendations for healthcare professionals (who prescribe, dispense, or review medicines or who have a role in making decisions about medicines with patients), under the following broad headings:

- *Patient involvement in decisions about medicines* (communication, increased patient involvement, understanding the patient's knowledge, beliefs and concern about medicines, providing information)
- *Supporting adherence* (assessing adherence, interventions to increase adherence)

- *Reviewing medicines* and
- *Communication between healthcare professionals* (NICE, 2009).

Thus, according to NICE, health professionals should involve patients in decisions about their medicines by making sure they communicate with them effectively. This includes adopting a style that gives the patient the opportunity to become involved in the conversation, asking open-ended questions to uncover their concerns, and encouraging the patient too to ask questions. Specifically, the health professional should include a conversation about what the patient hopes a new treatment will achieve, their views and concerns about the medication, and a discussion about the condition and how the medication will influence this, including the pros and cons. They should accept that the patient ultimately has the right to decide not to take the medication. Health professionals should also be aware that the patients might want to discuss a range of issues such as what happens if they are non-adherent, how they might reduce or stop longstanding medication, and how to make a choice between which of different medications to take. In due course, health professionals should assess the patient's adherence to their medication by asking, in a non-judgemental way, about their medication taking, for example whether in the past week they have missed any doses. If the patient is not adhering to their medication, health professionals should tailor any intervention they offer to the specific difficulties the patient is experiencing as well as their preferences. If side-effects are a particular problem for the patient, then health professionals should allow the patient to make an informed choice about how to deal with these by discussing the benefits as well as the side-effects of the medication. The dose taken may need to be adjusted, the medication switched to another drug, or a different strategy might be needed, such as changing the timing of when the medication is taken.

NICE published another relevant guideline, on medicines optimisation, in 2015 (NICE Medicines and Prescribing Centre, 2015). Also in line with a client-centred approach, medicines optimisation is defined as '*a person-centred approach to safe and effective medicines use, to ensure people obtain the best possible outcomes from their medicines.*' This guideline recommends carrying out medication reviews, as well as using self-management plans and patient decision aids during medicines-related consultations. Similar to the NICE guidelines on medicines adherence, healthcare professionals completing medication reviews as part of medicines optimisation are asked to take into account the patient's (and family members' or carers', where appropriate) views and understanding about their medicines as well as concerns, questions or problems they have with their medicines. Both of the NICE guidelines cited here are directed at health professionals who have competent knowledge and expertise about prescribing and medicines, such as doctors, nurses and pharmacists. But these health professionals often lack the psychological knowhow that underpins behaviour-change practices. One reasonable proposal to address this gap would be for closer, multi-disciplinary working that brings together the medicinal knowhow of pharmacists with the psychological expertise of practitioner psychologists to better support patients with their medication needs.

How do these guidelines help us respond to the 60-year old female whose case I outlined at the start of this article? There are a number of issues to consider. It is clear that the patient is experiencing side-effects that she considers to be detrimental to her quality of life. In addition, she has been unable to discuss her concerns with her GP, whom she considers has no interest in her cancer treatment. These concerns are likely to lead the patient to become 'non-persistent' with her medication, discontinuing the course of treatment early without first exploring her concerns with a health practitioner. The initial action then is to have a client-centred discussion with the patient in order to further explore her beliefs about the medication, its benefits and also the extent of concerns she has with the side-effects. A

practitioner psychologist would need to communicate with the other professionals involved in this patient's care, for example the GP, in order to explain the patient's beliefs, concerns and preferences, and suggest a medication review. During a medication review the patient may agree for her medication to be switched to another hormonal treatment or she may decide with the GP to stop taking the medication altogether. The key is the concordant approach that allows that open discussion and a joint decision about the medication to be reached with the patient.

I posed a question earlier about progress made in relation to understanding and tackling medication non-adherence. Arguably, the goal of treatment should be to empower patients to self-manage their chronic illness. In this sense, current advice focusses on recognising individual differences and providing a concordant, client-centred solution rather than a one-size-fits-all approach. But the problem of medication non-adherence remains a huge societal burden and much progress remains to be made in the field. Future research, for example, could examine the specific detail of a successful client-centred approach using methodology such as conversation analysis. The rapid advent of technology-enabled adherence services too provides considerable opportunity for ongoing research in the field. Currently, the best opportunity for providing adherence-focussed conversations, however, is at the point of prescribing and dispensing medication. Therefore, there is strong justification for asking the British Psychological Society and the different medical, pharmacy and nursing professional representative bodies to work together to improve the psychological knowhow of the wider group of professionals in the field including the prescribing and pharmacy workforce.

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Bibliography

Demonceau, J., Ruppar , T., Kristanto, P., Hughes, D., Fargher, E., Kardas, P., . . . Vrijens, B. (2013). Identification and Assessment of Adherence-Enhancing Interventions in Studies Assessing Medication Adherence Through Electronically Compiled Drug Dosing Histories: A Systematic Literature Review and Meta-Analysis. *Drugs, 73*(6), pp. 545–562.

DiMatteo, R., Giordani, P., Lepper, H., & Croghan, T. (2002). Patient Adherence and Medical Treatment Outcomes: A Meta-Analysis. *Med Care, 40*(9), pp. 794-811.

Dodds, F., Rebair-Brown, A., & Parsons, S. (2000). A systematic review of randomized controlled trials that attempt to identify interventions that improve patient compliance with prescribed antipsychotic medication. *Clin Eff Nurs, 4*(2), pp. 47-53.

Gadkari , A., & McHorney , C. (2012). Unintentional non-adherence to chronic prescription medications: How unintentional is it really? *BMC Health Serv Res, 12*. doi:10.1186/1472-6963-12-98

George, J., Mackinnon, A., Kong, D., & Stewart, K. (2006). Development and validation of the Beliefs and Behaviour Questionnaire (BBQ). *Patient Educ Couns, 64*(1-3), pp. 50-60.

Hahn, S., Park, J., Skinner, E., Yu-Isenberg, K., Weaver, M., Crawford, B., & Flowers, P. (2008). Development of the ASK-20 adherence barrier survey. *Curr Med Res Opin, 24*(7), pp. 2127-2138.

Horne, R., Chapman, S., Parham, R., Freemantle, N., Forbes, A., & Cooper, V. (2013). Understanding Patients' Adherence-Related Beliefs about Medicines Prescribed for Long-Term Conditions: A Meta-Analytic Review of the Necessity-Concerns Framework. *PLoS One, 8*(12), p. e80633. doi:doi:10.1371/journal.pone.0080633

Horne, R., Weinman, J., Barber, N., Elliott, R., Morgan, M., Cribb, A., & Kellar, I. (2005). *Concordance, adherence and compliance in medicine taking: Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R & D (NCCSDO).* Brighton: Centre for Health Care Research.

Horne, R; Weinman, J. (1999). beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness - processes and applications. *J Psychosom Res, 47*, pp. 555-567. doi:10.1016/s0022-3999(99)00057-4

Horne, R; Weinman, J; Hankins, M. (1999). The Beliefs about Medicines Questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health, 14*(1), pp. 1-14. doi:10.1080/08870449908407311

Jackson, C., Eliasson, L., Barber, N., & Weinman, J. (2014). Applying COM-B to medication adherence: A suggested framework for research and interventions. *The European Health Psychologist, 16*(1), pp. 7-17.

Kardas, P., Lewek, P., & Matyja, M. (2013). Determinants of patient adherence: a review of systematic reviews. *Front Pharmacol, 4*, p. 91. doi:10.3389/fphar.2013.00091

Kripalani, S., Yao, X., & Haynes, B. (2007). Interventions to Enhance Medication Adherence in Chronic Medical Conditions. *Arch Intern Med., 167*(6), pp. 540-549. doi:10.1001/archinte.167.6.540.

McHorney, C. (2009). The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. *Curr Med Res Opin, 25*(1), pp. 215–238. doi:10.1185/03007990802619425

Michie, S., van Stralen, M., & West, R. (2011). The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implement Sci, 6*, p. 42. doi:10.1186/1748-5908-6-42

NICE. (2009). *Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence.* National Institute for Health and Care Excellence.

NICE Medicines and Prescribing Centre. (2015). *Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes.* Manchester: National Institute for Health and Care Excellence.

Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., . . . Haynes, R. (2014, November 20). Interventions for enhancing medication adherence (Review). *Cochrane Database Syst Rev*. doi:10.1002/14651858.CD000011.pub4

Pound, P., Britten, N., Morgan, M., Yardley, L., Pope, C., Daker-White, G., & Campbell, R. (2005). Resisting medicines: a synthesis of qualitative studies of medicine taking. *Soc Sci Med, 61*(1), pp. 133-155.

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action.* Geneva: World Health Organisation.

Simpson, S., Eurich, D., Majumdar, S., Padwal, R., Tsuyuki, R., Varney, J., & Johnson, J. (2006). A meta-analysis of the association between adherence to drug therapy and mortality. *BMJ, 333*(15).

Svarstad, B., Chewning, B., Sleath, B., & Claesson, C. (1999). The Brief Medication Questionnaire: a tool for screening patient adherence and barriers to adherence. *Patient Educ Couns, 37*(2), pp. 113-124.

van Dulmen, S., Sluijs, E., van Dijk, L., de Ridder, D., Heerdink, R., & Bensing, J. (2007). Patient adherence to medical treatment: a review of reviews. *BMC Health Serv Res, 7*, p. 55. doi:10.1186/1472-6963-7-55

Vermeire, E., Hearnshaw, H., Van Royen, P., & Denekens, J. (2002). Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther, 26*(5), pp. 331-342.

Vrijens, B., De Geest, S., Hughes, D., Przemyslaw, K., Demonceau, J., Ruppar, T., . . . for the ABC Project Team. (2012). A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol, 73*(5), pp. 691–705.

Willey, C., Redding, C., Stafford, J., Garfield, F., Geletko, S., Flanigan, T., . . . Caro , J. (2000). Stages of change for adherence with medication regimens for chronic disease: development and validation of a measure. *Clin Ther, 22*(7), pp. 858-871.

Yeaw, J., Benner, J., Walt, J., Sian, S., & Smith, D. (2009). Comparing Adherence and Persistence Across 6 Chronic Medication Classes. *J Manag Care Pharm, 15*(9), pp. 728-740.